## REMARKS

### I. Status of the Claims

Claims 1-76 were filed with the application, and claims 21-76 were canceled in a preliminary amendment. In response to the restriction requirement which the examiner imposed, Applicants elected, without traverse, to prosecute claims 1-4 and 7-20, *i.e.*, the Group I claims. Claims 1-4 and 7-20 are thus under examination and stand rejected, variously under 35 U.S.C. §112, first paragraph, 35 U.S.C. §102 and 35 U.S.C. §103. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

### II. Objections

The examiner has objected to the specification as failing to provide a compliant sequence listing. **[INSERT]**

### III. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-4 and 7-20 are rejected under the first paragraph of §112 as lacking an adequate written description for the genus of peptides comprising the sequence KCCYSL. Applicants traverse.

The examiner's entire argument boils down to three issues: (a) that applicants have only exemplified a targeting agent consisting of KCCYSL; (b) that the claims encompass peptides up to 100 residues, of which 94 can be unspecified; and (c) that extraneous residues attached to KCCYSL might block the access of KCCYSL to its target or otherwise hinder its function. From this, the examiner concludes that one of ordinary skill in the art would not find that applicants were in possession of the invention and presently claimed.

Addressing these issues, applicants submit that (a) and (c) speak far more to issues of ***enablement*** than they do to written description, and thus are not properly raised as a complete *Wands* analysis is lacking from his action.. However, it is worth noting that even if there were some merit to (c), the inclusion of a few inoperable species does not render a generic claim non-enabled.

Turning to (b), applicants submit that the examiner has not properly applied the controlling legal precedent to the fact of the present situation. While applicants' claims do encompass non-specified subject matter, it is ***not*** the case that the claim lacks structural definition which is central to the examiner's argument. To the contrary, the claims specify sufficient structure to be both novel and non-obvious over the cited art, as discussed above. Moreover, whenever one of skill in the art observes a given peptide motif, it is ***immediately*** apparent that one can "link" such sequences to ***other*** peptides for a variety of purposes, including targeting sequences, stabilizing sequences, and a host of others. For example, the specification discusses the fact that variants of KCCYSL may be prepared, and includes a large section on linkers that can be utilized to attach various sequences to this peptide.

Thus, where the claims merely encompass various known features, in addition to a novel and non-obvious peptide sequence, these known features need not be specified in any detail. Because structure and specificity have been provided it in the form of KCCYSL, applicants have described their invention sufficiently to comply with §112, first paragraph. In light of this disclosure, and the understanding of the skilled artisan, this rejection makes no sense.

In short, the fact that applicants' claim covers both a large number of possible sequences that could be attached to KCCYSL, and the fact that only a single particular sequence is provided, do not render the claims of the present application lacking in written description. As

the PTO's reviewing court has said, "The Board erred in refusing to consider the state of the scientific knowledge, as explained by both parties, and in declining to consider the separate scope of each of the claims.... The 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. Both Eshhar and Capon explain that this invention does not concern the discovery of gene function or structure, as in *Lilly*. The chimeric genes here at issue are prepared from known DNA sequences of known function. The Board's requirement that these sequences must be analyzed and reported in the specification does not add descriptive substance. The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes." *Capon v. Eshhar*, 418 F.3d 1349, 1360 (Fed. Cir. 2005). Here, the unnamed sequences are ***not*** the subject of the invention, but may merely add to that which ***is*** the invention – SEQ ID NO:1.

Though not required, applicants now provide the declaration of Dr. Susan L. Deutscher. A collaborator with the inventors, Dr. Deutscher has used a radiolabeled KCCYSL peptide analog to image breast and prostate tumors in mouse models of disease. To effectively use the peptide KCCYSL for tumor targeting, she indicated that it was modified it to contain a radiometal chelator (DOTA) and a spacer peptide sequence (Gly-Ser-Gly) to yield DOTA-GSG-KCCYSL. The addition of the GSG linker peptide improved peptide binding of the erbB-2 receptor up-regulated on the tumor cells. This provides a clear example of how and why other sequences are linked to KCCYSL.

In addition, she states that MAP-4 and MAP-8 constructs of KCCYSL were made to to improve its affinity. The MAP-4 and MAP-8 molecules contain 4 and 8 copies of GSG-

KCCYSL linked via a lysine tree. Multiple copies of the KCCYSL linker via branched peptides showed much higher affinity for cancer cells than the single KCCYSL sequence. In addition, the KCYSL sequence has also been incorporated into hetero-MAP constructs, where a MAP contained two GSG-KCCYL sequences and two P30 TF antigen binding peptides linked together in one peptide. This allows targeting of tumor antigens on the cell at the same time, improving specificity and affinity.

Finally, Dr. Deutscher reports that she and the inventors are currently synthesizing a single polypeptide with two copies of KCCYSL in it. The peptide has the sequence DOTA-GSG-KCCYSL-(GSG)3-KCCYSL. This bi-dentate molecule will be compared to the MAP constructs to determine which presentation yield the best binding affinity and in vivo pharmacokinetics. Moreover, since they have used the KCCYSL sequence as a monomer, in complex homo- or hetero-MAP constructs with up to 8 copies, and in multiple representations in a single polypeptide, it is clear that this peptide sequence can be incorporated into larger peptide, and even macromolecules, and still retain its erbB-2 targeting properties.

Based on the preceding explanation of the claims, the supporting citations to the specification, the controlling case law, and the evidentiary submission included herewith, applicants respectfully submit that the challenge to the written description of the present claims is not well-founded. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

## IV. Rejection Under 35 U.S.C. §102(a)

Claims 1, 2 and 7-13 are rejected as lacking as anticipated by Karasseva *et al.* (2002). As explained in the attached "Katz" declaration under 37 C.F.R. §1.132, the non-inventor authors

did not contribute to the concept of the invention as described in the reference and are thus not properly named as inventors. Moreover, because the cited reference reflects the intellectual contributions of the present inventor, the reference is not "by another" and hence fails to qualify as prior art under 35 U.S.C. §102(a). Reconsideration and withdrawal of the rejection, in light of this submission, is therefore respectfully requested.

## V. Rejection Undre 35 U.S.C. §103

Claims 1-4 and 7-20 are rejected under §103 as obvious over Karasseva *et al.* in view of Thakur *et al.* (2000) and Langer *et al.* (2001). As explained above, Karasseva *et al.* is not prior art against the instant application. As such, reconsideration and withdrawal of the rejectionis also respectfully requested.

## VI. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. The examiner is invited to contact the undersigned attorney at (512) 536-3118 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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